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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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7590 10/13/2009  
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EXAMINER
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MABRY, JOHN

ART UNIT	PAPER NUMBER
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1625

MAIL DATE	DELIVERY MODE
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10/13/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/576,971	<b>Applicant(s)</b> SURI ET AL.	
	<b>Examiner</b> JOHN MABRY	<b>Art Unit</b> 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 26 May 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 64-77 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 64-77 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

***Examiner's Discussion of Claims***

Applicant's response on May 24, 2009 filed in response to the Office Action dated February 24, 2009 has been received and duly noted.

In examined claims dated April 25, 2006 where claims 1-43 were cancelled and claims 44-63 were new, Applicant primarily claimed "an improved method" for preparing montelukast acid or salt in an amorphous form. Claims were primarily drawn toward a step-wise synthetic "method for the preparation of montelukast acid or salt".

The most current set of claims dated May 26, 2009 where claims 1-63 are cancelled and claims 64-77 are new, wherein new claims are drawn to "a process for purification" and "a process for isolation" of montelukast acid, salts thereof, in amorphous and crystalline forms. The only claims in claims set dated April 25, 2006 that were remotely close to the most current set of claims (dated May 26, 2009) are dependent claims were claims 50-63.

In view of this response, the status of the rejections/objections of record is as follows:

***Status of the Claims***

Claims 64-77 are pending and rejected.

Claims 1-63 have been cancelled.

***Response to Applicant's Remarks***

***Claim Objection***

Objection to claim 47 regarding the term “diol” has been overcome in view of Applicant cancelling the claim.

***35 USC § 112 Rejection(s)***

The 112-2<sup>nd</sup> rejection of claims 47, 48, 53 and 54 regarding “C≡8” has been overcome in view of Applicant cancelling the claims.

The 112-2<sup>nd</sup> rejection of claim 47 regarding the “preferably” have been overcome in view of Applicants cancelling the claims.

***Claim Rejections - 35 USC § 102***

Claims 44-63 rejections are withdrawn under 35 U.S.C. 102(b) as being anticipated Bhupathy et al (US 6,320,052) in view of Applicant's cancelling claims.

An action on the merits of claims 64-77 is contained herein below.

**DETAILED ACTION**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 64-75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "substantially pure" in claim 64 and 70 is a relative term which renders the claim indefinite. The term "substantially pure" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. What does this term mean? Are there varying degrees of pure? Where does the specification define such term?

Regarding claims 47, the phrase "substantially pure" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 64-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhupathy et al (US 6,320,052).

The instant application claims a process for purification of montelukast dicyclohexylamine salt (X) comprising of crude X stirring in an organic solution in which the organic solution is toluene and ethyl acetate. The suspended solid is filtered as a wet cake and dried as a substantially pure form of montelukast dicyclohexylamine salt (X).

#### ***Scope & Content of Prior Art MPEP 2141.01***

Crystalline form of montelukast dicyclohexylamine salt of formula X is obtained by crystallization from toluene/heptane. The combined crystals are diluted with additional toluene and heptane is added to the toluene solution (see columns 8, lines 45-54).

***Differences between Prior Art & the Claims MPEP 2141.02***

Bhupathy differs from the instantly claimed invention by the solvent system used during the purification process: (a) Bhupathy's toluene/heptane versus Applicant's toluene/ethyl acetate and (b) Bhupathy does not specifically disclose recrystallization and isolation step as claim.

***Prima Facie Obviousness, Rational & Motivation MPEP 2142-2413***

It would be obvious for an artisan of ordinary skill to:

(a) try a slightly different solvent system as claimed. However, with the guidance of the disclosure of Bhupathy, a skill artisan would be motivated to use the solvent system as claimed – toluene/ethyl acetate.

Bhupathy teaches that the montelukast dicyclohexylamine salt can be recrystallized from an organic solvent, preferably toluene, an ester such as ethyl acetate or a mixture thereof (see column 9, lines 20-25). This is clear guidance that the claimed solvent system used to purify the montelukast dicyclohexylamine salt can be achieved using Bhupathy.

(b) to isolate a solid/precipitate from its solvent system by filtering and drying under vacuum. This is typical organic laboratory practice which is supported by Harwood and Moody in *Experimental Organic Chemistry: Principles and Practice*, 1989, pages 127-138 – see entire reference provided.

Harwood and Moody clearly and comprehensively describe the crystallization process. Fig. 3.37 illustrates the routine process of purifying a compound via

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crystallization, filtration and drying of solids (see page 128). Selection of crystallization solvents are described and listed in Table 3.6 i.e. toluene and ethyl acetate and motivation for use of mixed solvent systems for crystallization (see second complete paragraph on page 130).

The above differences are simply the adjustment of particular conventional working conditions (e.g. determining result effective amounts of the ingredients beneficially taught by the cited reference), as well as adjustment of reaction temperature, reaction time and use of solvents, is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan (*In re Mostovych*, Weber, Mitchell and Aulbach, 144 USPQ 38). Accordingly, these types of modifications would have been well within the purview of the skilled artisan and no more than an effort to optimize results.

Claims 70-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhupathy et al (US 6,320,052).

The instant invention claims a process for the isolation of montelukast acid in solid form which comprises of reacting montelukast dicyclohexylamine salt (X) with aqueous acetic acid in an organic solvent such as toluene and ethylacetate. The organic solution is then stirred 10-40°C, separated, filtered and dried.



***Scope & Content of Prior Art MPEP 2141.01***

Bhupathy discloses a process of reacting the montelukast dicyclohexylamine salt (X) with aqueous acetic acid in an organic solvent such as toluene, an ester such as ethyl acetate or a mixture thereof (see column 9, lines 20-25). This suspension at room temperature is added an aqueous solution of an organic acid, preferably acetic acid (see column 9, lines 25-28).

***Differences between Prior Art & the Claims MPEP 2141.02***

Bhupathy differs from the instantly claimed invention by the solvent system used during the purification process: (a) Bhupathy's toluene/heptane versus Applicant's toluene/ethyl acetate and (b) Bhupathy does not specifically disclose recrystallization and isolation step as claim.

***Prima Facie Obviousness, Rational & Motivation MPEP 2142-2413***

It would be obvious for an artisan of ordinary skill to:

(a) try a slightly different solvent system as claimed. However, with the guidance of the disclosure of Bhupathy, a skill artisan would be motivated to use the solvent system as claimed – toluene/ethyl acetate.

Bhupathy teaches that the montelukast dicyclohexylamine salt can be recrystallized from an organic solvent, preferably toluene, an ester such as ethyl acetate or a mixture thereof (see column 9, lines 20-25). This is clear guidance that the claimed

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solvent system used to purify the montelukast dicyclohexylamine salt can be achieved using Bhupathy.

(b) to isolate a solid/precipitate from its solvent system by filtering and drying under vacuum. This is typical organic laboratory practice which is supported by Harwood and Moody in *Experimental Organic Chemistry: Principles and Practice*, 1989, pages 127-138 – see entire reference provided.

Harwood and Moody clearly and comprehensively describe the crystallization process. Fig. 3.37 illustrates the routine process of purifying a compound via crystallization, filtration and drying of solids (see page 128). Selection of crystallization solvents are described and listed in Table 3.6 i.e. toluene and ethyl acetate and motivation for use of mixed solvent systems for crystallization (see second complete paragraph on page 130).

The above differences are simply the adjustment of particular conventional working conditions (e.g. determining result effective amounts of the ingredients beneficially taught by the cited reference), as well as adjustment of reaction temperature, reaction time and use of solvents, is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan (*In re Mostovych*, Weber, Mitchell and Aulbach, 144 USPQ 38). Accordingly, these types of modifications would have been well within the purview of the skilled artisan and no more than an effort to optimize results.

Claims 76-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhupathy et al (US 6,320,052).

The instant invention claims a process for the preparation of montelukast acid by dissolving the solid motelukast acid in methanol in the presence of a sodium source, removing methanol under vacuum to obtain a solid residue and triturating the solid residue with an aliphatic hydrocarbon. Then finally filtering the solid and drying under vacuum.

#### ***Scope & Content of Prior Art MPEP 2141.01***

Bhupathy discloses a process of reacting the montelukast acid in an organic solution then exposed to a sodium source - sodium hydroxide in ethanol. The montelukast sodium salt was then filtered and allowed to dry.

#### ***Differences between Prior Art & the Claims MPEP 2141.02***

Bhupathy differs from the instantly claimed invention by the solvent system used during the purification process: (a) Bhupathy's disclosure did not evaporate alcohol solvent then triturate with aliphatic hydrocarbon and (b) Bhupathy used ethanol instead of methanol.

#### ***Prima Facie Obviousness, Rational & Motivation MPEP 2142-2413***

It would be obvious for an artisan of ordinary skill to:

- (a) try to isolate the desire solid in different order of step(s).
- (b) to use methanol instead of ethanol.

The above differences are simply the adjustment of particular conventional working conditions (e.g. determining result effective amounts of the ingredients beneficially taught by the cited reference), as well as adjustment of reaction temperature, reaction time and use of solvents, rearrangement of step to isolate, is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan (*In re Mostovych*, Weber, Mitchell and Aulbach, 144 USPQ 38). Accordingly, these types of modifications would have been well within the purview of the skilled artisan and no more than an effort to optimize results.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### ***Conclusion***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John Mabry, PhD whose telephone number is (571) 270-1967. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's primary examiner can be reached at (571) 272-0684, first, or the Examiner's supervisor,

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Janet Andres, PhD, can be reached at (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/John Mabry/  
Examiner  
Art Unit 1625

/Rita J. Desai/  
Primary Examiner, Art Unit 1625